

CLAIMS

What is claimed is:

1. A purified antibody which preferentially binds an ECRTP/DEP-1, or a fragment or derivative of the antibody.

5 2. The antibody of claim 1, which preferentially binds an ectodomain of the ECRTP/DEP-1.

10 3. The antibody of claim 2, which preferentially binds an eight amino acid epitope having the sequence QSRDTEVL, or an eight amino acid epitope having an analog sequence of the sequence QSRDTEVL, of the ECRTP/DEP-1 ectodomain.

15 4. The antibody of claim 1, which is a monoclonal antibody, or fragment or derivative thereof.

5. The antibody of claim 4, which is monoclonal antibody ECRTPAb-1, having a molecular weight of about 150 kDa and which preferentially binds to an ectodomain of the ECRTP/DEP-1.

20 6. The antibody of claim 4, further characterized as having the immunoreaction characteristics of a monoclonal antibody produced by a hybridoma cell line having ATCC accession number HB12570.

7. The antibody of claim 6, where the monoclonal antibody is a monoclonal antibody produced by a hybridoma cell line having ATCC accession number HB12570.

8. The antibody of claim 1, wherein the antibody is humanized.

9. The antibody of claim 8, which preferentially binds to an ectodomain of the ECRTP/DEP-1.

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10. The antibody of claim 9, which preferentially binds an eight amino acid epitope having the sequence QSRDTEVL, or an eight amino acid epitope having an analog sequence of the sequence QSRDTEVL, of the ECRTP/DEP-1 ectodomain.

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5 11. The antibody of claim 8, wherein the humanized antibody comprises monoclonal antibody ECRTPAb-1, having a molecular weight of about 150 kDa and which preferentially binds to an ectodomain of the ECRTP/DEP-1.

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10 12. The antibody of claim 8, wherein the humanized antibody is further characterized as having the immunoreaction characteristics of a monoclonal antibody produced by a hybridoma cell line having ATCC accession number HB12570.

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15 13. The antibody of claim 12, where the monoclonal antibody is monoclonal antibody produced by a hybridoma cell line having ATCC accession number HB12570.

14. The antibody of claim 1, in a pharmaceutically acceptable diluent or excipient.

15. A pharmaceutical composition comprising an isolated and purified biologically active ECRTP/DEP-1 polypeptide, or amide, conjugated, cyclized, 20 fragment, chemically modified embodiment thereof, and a pharmaceutically acceptable carrier.

16. The pharmaceutical composition of claim 15, wherein the polypeptide further comprises an ectodomain of the ECRTP/DEP-1.

17. The pharmaceutical composition of claim 16, wherein the polypeptide further comprises an eight amino acid epitope of the ectodomain of the ECRTP/DEP-1, the epitope having the sequence QSRDTEVL, or an eight amino acid epitope of the ectodomain of the ECRTP/DEP-1 having an 5 analog of the sequence QSRDTEVL.

18. The pharmaceutical composition of claim 15, further comprising a cell expressing the ECRTP/DEP-1 polypeptide.

19. A method of screening a candidate substance for an ability to modulate a receptor tyrosine phosphatase, the method comprising:

- 10 (a) establishing a test sample comprising a receptor tyrosine phosphatase;
- (b) administering a candidate substance to the test sample; and
- (c) measuring a receptor tyrosine phosphatase biological activity in the test sample;
- 15 (d) detecting phosphotyrosine residues on the receptor tyrosine phosphatase; and
- (e) determining that the candidate substance modulates the receptor tyrosine phosphatase if the receptor tyrosine phosphatase biological activity measured for the test sample is greater or less than the receptor tyrosine phosphatase biological activity measured for a control sample and if the amount of phosphotyrosine residues on the receptor tyrosine phosphatase is greater or less than an amount of phosphotyrosine residues on a receptor tyrosine phosphate derived from a control sample.

20. The method of claim 19, wherein the test and control samples further comprise a cell, and the receptor tyrosine phosphatase is expressed in the cell.

21. The method of claim 20, wherein the test and control sample 5 comprise cells expressing an ECRTP/DEP-1.

22. The method of claim 21, wherein the ECRTP/DEP-1 activity is selected from the group consisting of modulation of endothelial cell migration and proliferation, modulation of density induced growth arrest, modulation of angiogenesis and combinations thereof.

10 23. The method of claim 19, wherein the candidate substance further comprises a cell or cell lysate comprising a natural ligand for the receptor tyrosine phosphatase, and the method further comprises isolating the natural ligand for the receptor tyrosine phosphatase.

15 24. The method of claim 23, wherein the receptor tyrosine phosphatase comprises the ECRTP/DEP-1.

25. The method of claim 24, wherein the ligand is isolated by lysing the cells and passing the cell lysate over a column containing the ECRTP/DEP-1 bound to a solid phase matrix within the column.

20 26. The method of claim 24, wherein the ligand is isolated by constructing a cDNA library from the cells binding the ligand; transfecting the cDNA library into a cell line that does not exhibit binding of the ligand; screening the cell line for newly acquired specific binding; isolating DNA from cells exhibiting specific binding; and sequencing the isolated DNA to determine the DNA sequence for the ligand.

27. A recombinant cell line suitable for use in the assay of claim 19.

28. A method of screening a candidate substance for an ability to modulate EC RTP/DEP-1 biological activity, the method comprising:

5 (a) establishing a test sample comprising an EC RTP/DEP-1 polypeptide or fragment thereof;

(b) administering a candidate substance to the test sample; and

(c) measuring an interaction, effect, or combination thereof, of the candidate substance on the test sample to thereby determine the ability of the candidate substance to modulate EC RTP/DEP-1

10 biological activity.

29. The method of claim 28, wherein the test sample further comprises a cell expressing EC RTP/DEP-1, and wherein the step of measuring an interaction, effect, or combination thereof, of the candidate substance on the test sample further comprises:

15 (i) comparing the interaction, effect, or combination thereof, of the candidate substance on the test sample with the interaction, effect, or combination thereof, of the candidate substance on a cell not expressing EC RTP/DEP-1; and

(ii) determining that candidate compound modulates EC RTP/DEP-1

20 activity by demonstrating a lack of interaction, effect or combination thereof, of the candidate compound on cells not expressing EC RTP/DEP-1.

30. The method of claim 28, wherein said step of measuring an interaction, effect, or combination thereof, of the candidate substance on the

test sample further comprises measuring binding between the candidate substance and the test sample by:

- (i) contacting the candidate substance with an ECRTP/DEP-1 polypeptide or fragment thereof under conditions favorable to binding the candidate with an ECRTP/DEP-1 polypeptide or fragment thereof to form a complex therebetween; and
- (ii) detecting the complex.

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31. The method of claim 30, wherein the complex is detected via a label conjugated to the ECRTP/DEP-1 polypeptide or fragment thereof; via a labeled reagent that specifically binds to the complex subsequent to its formation; or via a competition assay with a substance known to bind the ECRTP/DEP-1 polypeptide or fragment thereof.

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32. The method of claim 30, wherein the ECRTP/DEP-1 polypeptide or fragment thereof is conjugated with a detectable label.

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33. The method of claim 32, wherein the step of detecting the complex further comprises:

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- (i) separating the complex from unbound labeled ECRTP/DEP-1 polypeptide or fragment thereof; and
- (ii) detecting the detectable label which is present in the complex or which is unbound.

34. The method of claim 30, wherein the ECRTP/DEP-1 polypeptide fragment is a ECRTP/DEP-1 ectodomain fragment.

35. The method of claim 34, wherein the ECRTP/DEP-1 ectodomain fragment comprises an eight amino acid epitope having the sequence n-QSRDTEVL-c.

36. The method of claim 30, wherein the candidate substance is an antibody, or derivative or fragment thereof.

37. The method of claim 36, wherein the candidate antibody, or derivative or fragment thereof, is derived from a recombinant phage-displayed antibody library.

38. A kit for use screening a candidate substance for an ability to modulate ECRTP/DEP-1 biological activity, the kit comprising a ECRTP/DEP-1 ectodomain polypeptide, or fragment thereof, contained in a first container.

39. The kit of claim 38, wherein the ECRTP/DEP-1 ectodomain polypeptide, or fragment thereof, comprises an eight amino acid epitope having the sequence n-QSRDTEVL-c.

40. The kit of claim 38, further comprising a solid phase support.

41. The kit of claim 40, where the ECRTP/DEP-1 ectodomain polypeptide, or fragment thereof, is immobilized to the solid phase support.

42. The kit of claim 38, further comprising a detectable label.

43. The kit of claim 41, wherein the detectable label is contained in another container or wherein ECRTP/DEP-1 ectodomain polypeptide, or fragment thereof, comprises the detectable label.

44. The kit of claim 43, wherein the detectable label is a radioactive label or an enzyme.

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